Remarks

The Office Action dated December 5, 2001 has been carefully reviewed and the foregoing amendments are made in response thereto. Applicants appreciate the Examiner's efforts in furthering the prosecution of this Application by granting an interview on March 14, 2002. In view of the discussion during the interview, the above amendments and the following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Applicants respectfully submit that no prohibited new matter has been introduced by the amendments. Written description support for the amended claims can be found throughout the specification. Specific support for incorporation of the term "free from sporozoite antigens" can be found on page 8, lines 15-17. Written description support for additional claims 24-37 can be found in original claims 1-23.

Summary of the Office Action

1. The rejection of claim 4 under 35 U.S.C. 112 (second paragraph) as being indefinite was withdrawn.

2. The rejection of claims 20-23 under 35 U.S.C. 112 (first paragraph) was maintained pending allowance of the claims and perfection of the deposit requirement.

3. The rejection of claims 1-8 and 16-17 under 35 U.S.C. 102(b) as being anticipated by McDonald *et al.* was maintained.

4. The rejection of claims 9-15 and 18-19 under 35 U.S.C. 103(a) as being unpatentable over McDonald *et al.* in view of Riggs *et al.* was maintained.

Rejections under 35 U.S.C. 112

The Office Action rejected claims 20-23 under 35 U.S.C. 112 (first paragraph) for failing to provide an enabling disclosure because the specification lacks complete deposit information for the clone CRY 104. Applicants respectfully request the Examiner hold this rejection in abeyance until allowable subject matter has been found with the understanding that the necessary information will be provided at such time.

Rejection under 35 U.S.C. 102(b)

Claims 1-8 and 16-17 were rejected under 35 U.S.C. 102(b) for allegedly being anticipated by McDonald *et al.* (1995). The Office Action purports that the cited reference discloses an IgG antibody, produced specifically against the oocyst wall (page 3, lines 11-13). As discussed in the Examiner interview of March 14, 2002, McDonald *et al.* (1995) discloses antibodies against oocyst antigens that were produced by the method of McDonald *et al.* (1991). This earlier reference discloses a method whereby intact oocysts are homogenized and subsequently injected into Balb/c mice for the generation of monoclonal antibodies (see page 253, lines 4-7). As each intact oocyst contains a sporozoite, the homogenate used in McDonald *et al.* (1991) contained sporozoite antigens, resulting in the formation of antibodies against sporozoites.

The method claims in the present application have been amended to provide the limitation that the oocyst wall preparation be free from any sporozoite antigens. There is no discussion in the cited reference, however, of any oocyst pretreatment with an agent so as to remove the surface layer of the oocysts to form an oocyst antigen preparation, nor of separation of internal sporozoite components prior to inoculation. In contrast, Applicants have found that in order to obtain a suitable oocyst wall antigen preparation, the oocyst wall should be separated from internal sporozoite components (see page 4, lines 1-7 of the specification).

Applicants also bring to the attention of the Examiner that claim 16 is drawn to an isolated IgG1 antibody produced by the method of claim 1. As discussed above, claim 1 now provides the limitation in step (b) that the oocyst wall preparation be free from sporozoite antigens. The cited reference discloses a single antibody of the IgG subclass designated 2C3 (see page 260, second column, line 14). Furthermore, Applicants note that the 2C3 antibody disclosed in McDonald *et al.* (1995) reacted with the whole sporozoite and the sporozoite surface (see page 263, first column, lines 1-2). Applicants therefore respectfully submit that McDonald *et al.* (1995) does not disclose an IgG1 antibody that specifically binds to oocyst wall antigens and does not bind to any internal sporozoite components. The antibodies of the present invention are incapable of specifically binding to sporozoite components because the animals were inoculated with a antigen preparation free of sporozoite components.

Rejection under 35 U.S.C. 103(a)

The Office Action maintained that claims 9-15 and 18-19 are unpatentable under 35 U.S.C. 103(a) over McDonald *et al.* (1995) in view of Riggs *et al.* (1994). The Office Action alleges that as Riggs *et al.* (1995) discloses immunization with purified oocysts, it can be reasonably concluded that the

preparation contained separation of at least part of the oocyst wall from internal sporozoites, thereby meeting all of the limitations of claim 9.

In response, Applicants have further amended claim 9 providing the limitation that the oocyst wall preparation be free of sporozoite antigens. In light of the amendment, Applicants submit that Riggs *et al.* (1994) does not disclose a method of preparing an oocyst wall free from internal sporozoites antigens and therefore, does not disclose all of the limitations of claim 9. As set forth on page 1130, second column, lines 34-35 of this publication, it is clear that the sonicated oocyst antigen preparation comprised oocyst walls, residual bodies and sporozoites. Furthermore, at page 1937, second column, lines 11-12, it is stated that the sonicated oocyst preparation used for inoculation contained sporozoites. Applicants have amended claim 9 to clearly indicate that the oocyst wall preparation be free from any sporozoite antigens.

Applicants therefore respectfully submit that Riggs *et al.* (1994) does not disclose the separation of "at least a part of the Cryptosporidium oocyst wall from the internal sporozoites to form an oocyst-wall preparation free from sporozoite antigens" as is required by step (a) in amended claim 9. For these reasons, Applicants respectfully submit 9-15 and 18-19 are clearly non-obvious over McDonald *et al.* (1995) in view of Riggs *et al.* (1994) and request that the rejection be withdrawn.

Conclusion

In view of the foregoing, Applicants respectfully request reconsideration and the timely allowance of the pending claims. Should the Examiner feel that there are any issues outstanding after consideration of this response, the Examiner is invited to contact Applicants' undersigned representative to expedite prosecution. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made" as required.

If there are any other fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. 1.136 not accounted for in the attached petition, such an extension is requested and the fee should also be charged to our Deposit Account No. 50-0310.

Respectfully submitted
Morgan, Lewis & Bockius LLP

Robert Smyth
Registration No. 50,801

Dated: **May 6, 2002**
Morgan, Lewis & Bockius LLP
Customer No. **009629**
1111 Pennsylvania Ave., N.W.
Washington, D.C. 20004
202-739-3000

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claim 1 has been amended as follows:

1. (Once Amended) A method of producing isolated IgG1 subclass antibodies reactive to the surface of *Cryptosporidium* oocysts, the method comprising:

(a) pretreating *Cryptosporidium* oocysts with a reagent so as to remove the surface layer of the oocysts to form an oocysts antigen preparation;

(b) separating the oocysts from the oocyst antigen preparation so as to obtain a separated oocyst antigen preparation free from sporozoite antigens and capable of eliciting a detectable IgG1 immune response in an animal to the surface of the oocyst;

(c) immunizing an animal with the separated oocyst antigen preparation so as to elicit an IgG1 response in the animal; and

(d) obtaining from the animal IgG1 antibodies reactive to the surface of *Cryptosporidium* oocysts.

Claim 9 has been amended as follows:

9. (Once Amended) A method of producing isolated IgG1 subclass antibodies reactive to the surface of *Cryptosporidium* oocysts, the method comprising:

(a) separating at least a portion of the *Cryptosporidium* oocysts wall from the internal sporozoites to form an oocyst-wall preparation free from sporozoite antigens;

(b) treating the separated oocyst-wall preparation so as to obtain an isolated oocyst wall antigen preparation free from sporozoite antigens capable of eliciting a detectable IgG1 immune response in an animal to the surface of the oocyst;

(c) immunizing an animal with the isolated oocyst wall antigen preparation so as to elicit an IgG1 immune response in the animal; and

(d) obtaining from the animal IgG1 antibodies reactive to the surface of *Cryptosporidium* oocysts.

Claim 13 has been amended as follows:

13. (Twice Amended) The method according to claim 9 wherein the treating step (b) comprises physically breaking up the [~~cell~~] oocyst wall.

Claim 22 has been amended as follows:

22. (Once Amended) The antibody according to claim [~~21~~] 20 wherein the IgG1 monoclonal antibody is produced by hybridoma CRY104.

New claims 24-37 have been added.